

8 June 2000

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

RE: Class II 510(k) exemption petition

To whom it may concern:

The undersigned submits this petition under section 510(m)(2) of the Food Drug and Cosmetic Act to request the Commissioner of Food and Drugs to reclassify the following device

Std. Nomenclature	Catheter, retention, barium enema with bag
Product Code	78FGD
Regulation Number	21CFR§876.5890

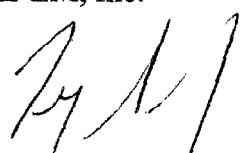
And by extension, barium enema retention enema tips sold alone, from Class II to Class II (exempt):

If there are any questions concerning this petition, please contact

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Director, Regulatory Affairs
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Sincerely,

E-Z-EM, Inc.


Terry S. Zisowitz, Esq.
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E-Z-EM, Inc. is a publicly held corporation whose shares are traded on the American Stock Exchange under the symbols EZEM.A and EZEM.B

00P-1343

CCP 1

A. ACTION REQUESTED

Add the following:

21CFR§876.5980(b)(3) – Class II (exempt) for the barium enema retention catheter with or without bag.

B. STATEMENT OF GROUNDS

1. Background – Barium sulfate has been used as a contrast agent for diagnostic radiographic imaging of the gastrointestinal tract since the early 1900s^{1,2,3,4,5,6} and possibly as early as the late 1800s^{2,5}. Barium sulfate is administered both orally and rectally. Rectal administration is accomplished using devices known at various times and in various places as pipes, bones, catheters, or enema tips. For the purposes of this discussion FDA's standard nomenclature terms "catheter" and "retention catheter" will be used to denote barium sulfate rectal catheters and barium sulfate rectal retention catheters, respectively.

Catheters, while numerous and in varied particulars of design, can be classified into two broad categories, specifically, those with inflatable cuffs on their tips designed to help the patient retain the barium sulfate in the bowl for the duration of the radiographic procedure (so called "retention catheters"), and those without said balloon cuffs, designed for procedures where the physician determines that the need to assist the patient in retaining the barium sulfate is not indicated (so called non-retention catheters). The basic designs of the two variants are similar, in fact, in many instances there are retention and non retention variants of the same catheter with the only difference between the two being 1) the addition of the inflatable cuff at the distal end of the catheter and 2) the addition of a second airway to allow for the inflation of the inflatable cuff. A cross-sectional diagram depicting the non-retention catheter (designated as "enema tip plain"), the retention catheter with the cuff not inflated (designated as "cuff not inflated"), and the retention catheter with the cuff inflated (designated as "cuff inflated") appears in Appendix 1.

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- 1 Bachem C, Günther H: Bariumsulfat als schattenbildendes Kontrastmittel bei Röntgenuntersuchungen. Zeiter Röntgenkunde Rad Forsch 1910; 12:369-376
 - 2 Canon WB: The passage of different foodstuffs from the stomach and through the small intestine. Am J Physiol 1904; 12:387-418
 - 3 Canon WB: Early use of the Röntgen ray in the study of the alimentary canal. JAMA 1914; 62:1-3
 - 4 Günther H: Bariumsulfat als schattenbildendes Kontrastmittel bei Röntgenuntersuchungen. Deutsch Med Wschr 1911; 37:717
 - 5 Hampton AO: A safe method for roentgen demonstration of bleeding duodenal ulcers. AJR 1937; 38:565-570
 - 6 Pels Rijcken TH et. al., Intraluminal Contrast Agents for MR imaging of the Abdomen and Pelvis. JMRI 1994; 4:291-300

2. REGULATORY

Disposable barium enema kits are considered to be Class I devices (product code 90FCD) while barium enema kits with retention catheters are considered to be Class II devices (product code 78FGD). E-Z-EM (hereinafter referred to as the petitioner), based on its long history of manufacturing and marketing both types of devices believes that there should be no difference in the premarket notification (PMN) requirements for these two types of devices and is hereby petitioning FDA to exempt barium enema bags with retention catheters, and by extension, the retention catheters themselves, from PMN requirements in accordance with the petition requirements outlined in 21 CFR§10.30.

The Food and Drug Administration Modernization Act of 1997 amended section 510(k) of the Food Drug and Cosmetic Act to exempt those class II devices which FDA determines, either on its own initiative or by petition of an interested party, do not require a 510(k) submission.

It is the petitioner's position that the degree of regulatory control required for the legal marketing of a retention catheter should not differ from that required for a non-retention catheter. The basis for the petitioner's belief is that there is no significant difference in use, indication, design, materials, labeling, or risks associated with the use of either device. Specifically, both are used to instill fluids into the alimentary tract; both are indicated for the administration of barium sulfate rectally in connection with a diagnostic radiographic imaging procedure of the GI tract; both have similar designs and differ only in the inflatable cuff/airway being present in the retention catheter and absent in the non-retention catheter, both are comprised on biocompatible elastomeric materials and both have similar labeling which includes a similar description of risks.

Risks associated with the use of such catheters include constipation, transient bacteremia, anaphylaxis secondary to latex content, pain discomfort, and perforation. Of these pain and discomfort are not considered to be clinically significant and are managed by simply selecting an appropriate sized catheter, using adequate lubrication, and correct placement (or repositioning). In a similar vein, constipation is more a function of the barium sulfate than of the catheter itself as evidenced by the same type of changes in bowel habits also being observed secondary to orally administered barium sulfate preparations. It should be noted that constipation secondary to barium sulfate administration is generally mild to moderate, not considered to be clinically significant, and is managed by instructing the patient to keep well hydrated both before and after the procedure, or in some cases, to use a mild laxative.

Transient bacteremia has been reported by Burhenne and Margoulis as being "probably common". The same authors state that while it is not customary to

take precautions in most cases, it is probably prudent to administer prophylactic antibiotics for those patients with mitral valve disease or who have undergone surgical valve replacement. It should be noted that no differentiation is made between the two types of catheters with respect to this potential risk and the management thereof.

Anaphylaxis secondary to the use of a latex containing catheter, or any latex containing medical device for that matter, is a potential source of serious risk of harm to patients, however, most manufacturers have reduced or eliminated this risk by removing the latex content from their devices (the petitioner has chosen to take this approach). Those manufacturers whose medical products still contain latex are now required by regulation to declare the presence of latex on their labeling, thereby increasing the learned intermediary's awareness of this potential risk. It is important to note that the risk of anaphylaxis secondary to latex exposure is not particular to the types of devices which are the subject of this petition, rather it is a risk that applies to any type of medical device, in any regulatory classification, which contains latex. There are, in fact, numerous devices which contain latex and are exempt from PMA or PMN notification requirements and for which FDA has determined that it is safe to market them as long as they accord with the latex "labeling requirements". Therefore, as it pertains to the risk of latex, exempting retention catheters from PMN requirements would not significantly change the risk to patients as compared to non-retention catheters or any other latex containing device.

Bowel perforation secondary to barium enema while potentially quite serious, is fortunately quite rare. The medical literature reports an incidence of bowel perforation secondary to barium enema to be in the 0.00004 to 0.0004^{7,8,9} range for all barium enemas (including those using retention and non-retention catheters). A review of the petitioner's complaint database for the last four completed calendar years (1996 through 1999) revealed a bowel perforation incidence of 0.0000007¹⁰. When one compares the incidence of bowel perforations for the retention and non-retention variants, the incidences are 0.0000006 and 0.00001, respectively, suggesting a statistically significant difference between the groups with the retention variant being "safer", however, since the number of bowel perforations in each group was very small (i.e. three and one, respectively) it is reasonable to conclude that these

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- 7 Williams SM, Harned RK: Recognition and Prevention of barium enema complications. *Curr Probl Diagn Radiol* 1991, Jul-Aug; 20(4):123-51
 - 8 Hakim NS, et.al: Management of barium enema-induced colorectal perforation. *Am Surg* 1992 Nov; 58(11):673-6
 - 9 Blakeborough A, Sheridan MB, Chapman AH: Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. *Clin Radiol* 1997 Feb; 52(2):142-8
 - 10 Calculated as the number of bowel perforations divided by the total number of procedures performed with E-Z-EM catheters (both retention and non-retention). The number of procedures is estimated using the number of units sold during the time period in question.

figures do not represent any significant difference, either statistically or clinically speaking.

Therefore, the petitioner concludes that the risk to patients is 1) not significantly different between the Class I catheter (non-retention) variant and the Class II catheter (retention) variant and 2) not likely to change if the retention variant is made exempt from PMN requirements as there is adequate control afforded by QSR.

FDA's guidance entitled, "Procedure for Class II Device Exemptions from Premarket Notification Guidance for Industry and CDRH Staff" describes the criteria the agency uses to determine which types of class II devices should be exempt from PMN requirements. It lists the following factors:

1. The device does not have a significant history of false or misleading claims or of risks associated with inherent characteristics of the device, such as device design or materials
2. characteristics of the device necessary for its safe and effective performance are well established;
3. changes in the device that could affect safety and effectiveness will either: (a) be readily detectable by users by visual examination or other means such as routine testing, before causing harm, e.g., testing of a clinical laboratory reagent with positive and negative controls; or (b) not materially increase the risk of injury, incorrect diagnosis, or ineffective treatment; and
4. any changes to the device would not be likely to result in a change in the device's classification.

The petitioner will address the above factors in the order in which they appear in the aforementioned guidance document. First, the petitioner is not aware of any significant history of false or misleading claims for the devices which are the subject of this petition, either for the devices manufactured by the petitioner or those manufactured by other manufacturers. Also, as discussed above, the risks associated with the use of these products is very low and is consistent with that of similar devices which are exempt from PMN requirements. Second, the characteristics of the device necessary for its safe and effective performance are well established as evidenced by the decades of use and greater than one billion procedures performed with devices whose characteristics and design are virtually unchanged from their inception. Third, as history indicates, changes to the device have been and are likely to continue to be evolutionary rather than revolutionary. Changes that could affect safety or effectiveness would either be readily apparent to the user through visual means or by routine testing and such changes would not be likely to materially increase the risk of injury, incorrect diagnosis, or ineffective treatment.

Fourth and finally, changes to the device would not be likely to result in the device being reclassified.

Therefore, it is the petitioner's conclusion that the retention catheter should be exempt from PMN requirements and the level of control afforded by QSR for a Class II device, exempt from PMN requirements are adequate to ensure the safe and effective use of the device.

C. ENVIRONMENTAL IMPACT

The petitioner is making a claim for categorical exemption for an Environmental Impact Statement under 21CFR §25.34 (Devices and Electronic Products).

D. ECONOMIC IMPACT

To be submitted if requested by the Commissioner.

E. CERTIFICATION

The undersigned certifies, that to the best knowledge and belief of the undersigned, the petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Signed: 

Name of petitioner: Terry S. Zisowitz
Vice President Legal/Regulatory Affairs
Legal Counsel

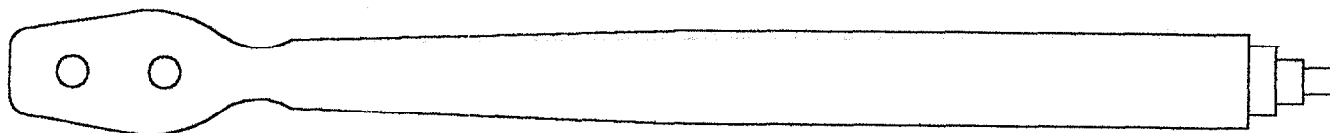
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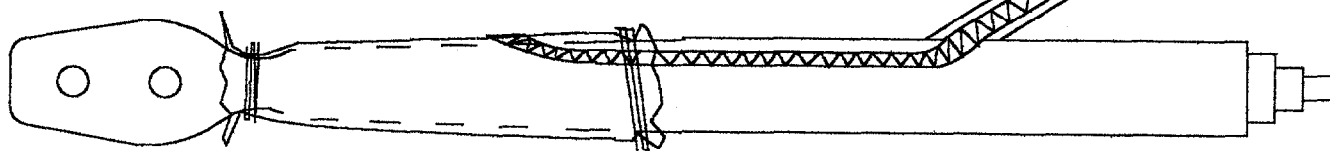
APPENDIX 1

ENEMA TIP PLAIN

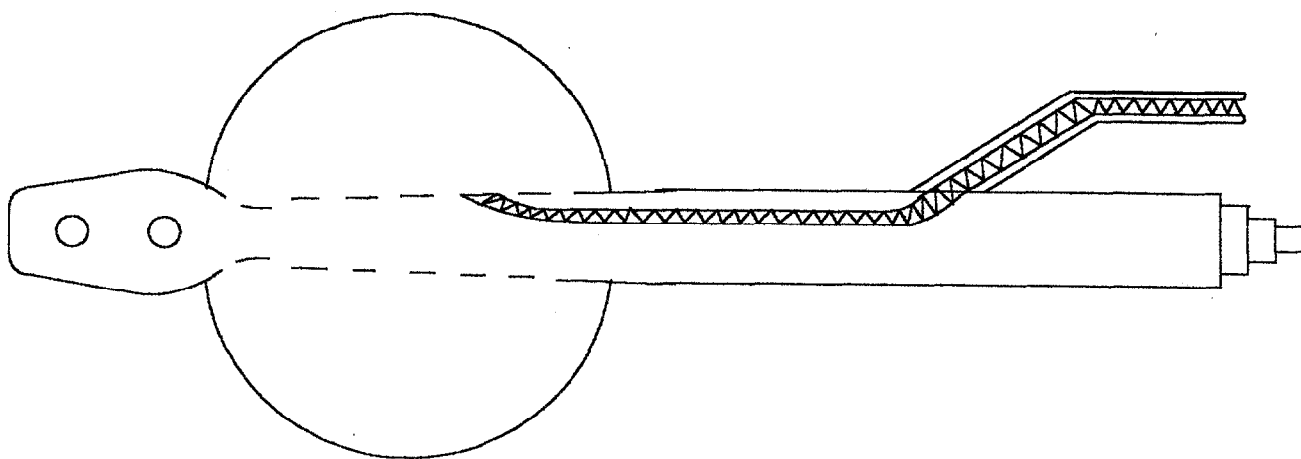


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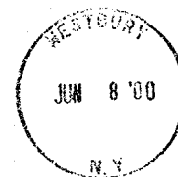
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CERTIFIED

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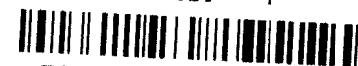
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